NHGRI Planning Workshop Recap- From Genome Function To Biomedical Insight: ENCODE And Beyond

National Advisory Council For Human Genome Research

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Functional Genomics Presentations

1 ENCODE Background
2 Functional Genomics Workshop
3 Functional Genomics Concepts

Functional Genomics Is Central To NHGRI Goals

Non-coding DNA is important for disease and gene regulation

- Vast majority of common disease associations lie outside of protein-coding regions
- Non-coding DNA variants are known to cause human diseases and alter human traits (FXS, ALS)

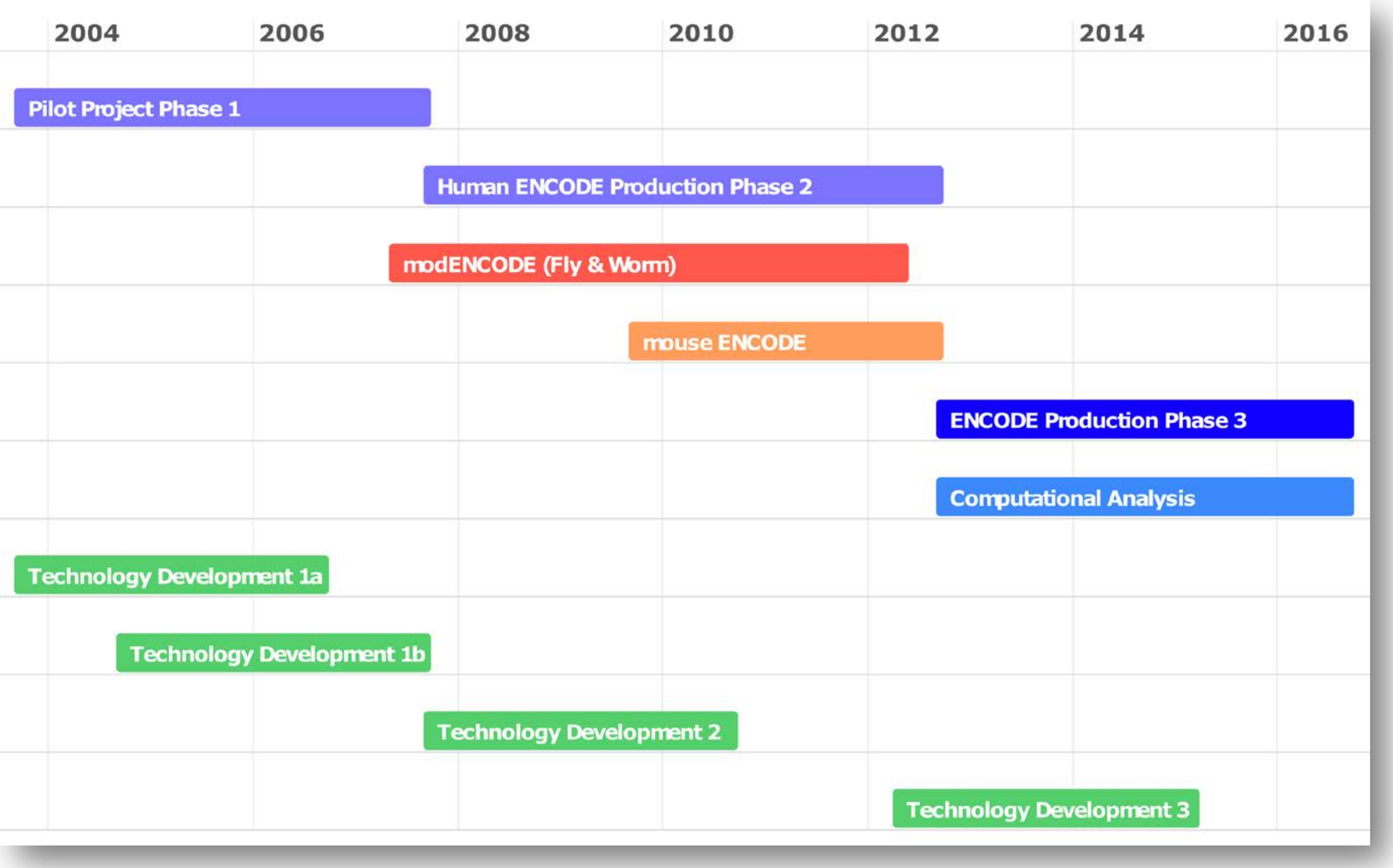
Functional information is needed to interpret the role of genetic variation in human disease, and to apply genomics in the clinic.

PMID: 22955828, PMID: 25439723
PMID: 17477822, PMID: 25679767

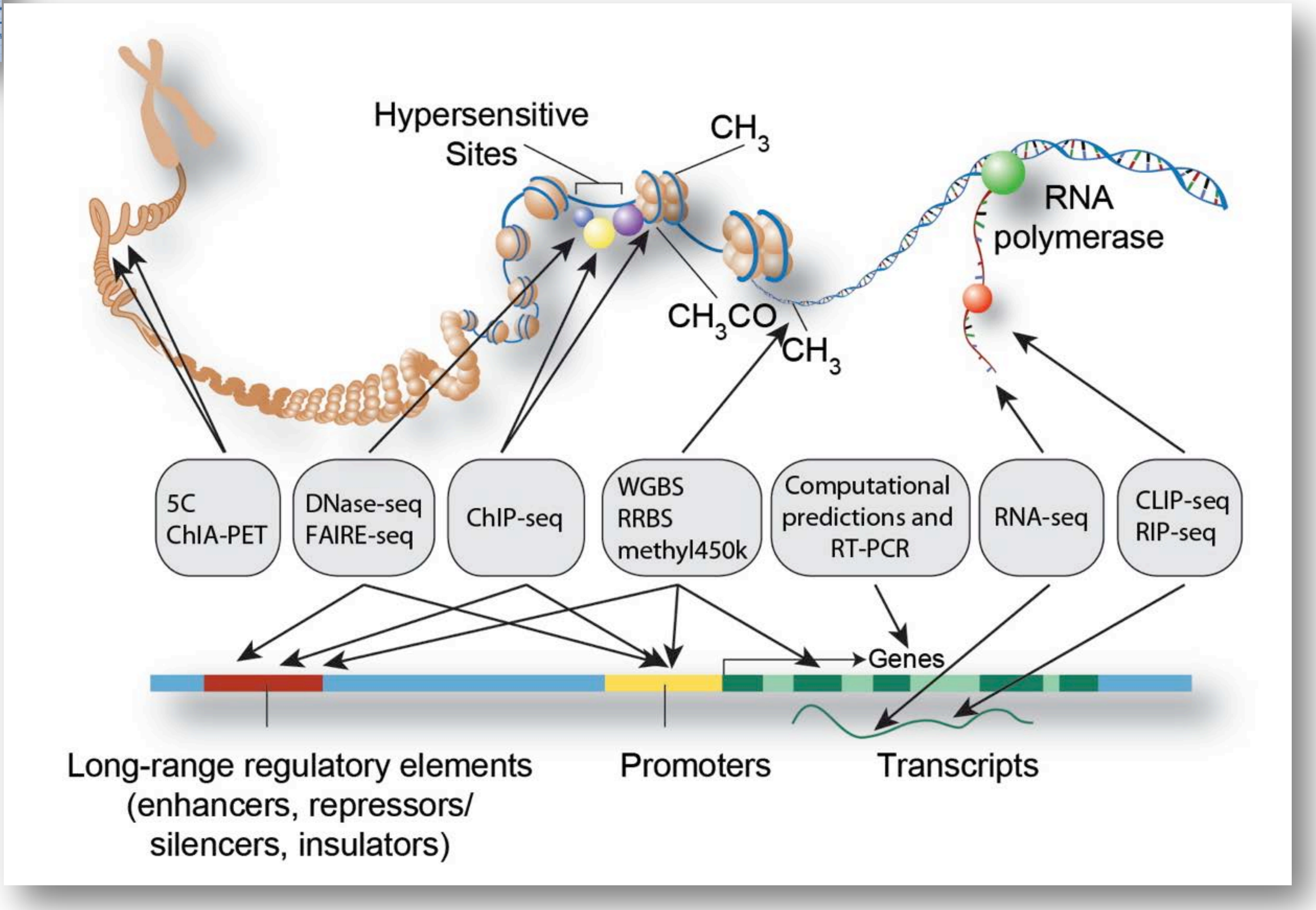
ENCODE: Encyclopedia Of DNA Elements

- Identify all candidate functional elements in the genome
- Make resource freely available to community for use in studies of:
  - genetic basis of disease
  - gene regulation

ENCODE Timeline



ENCODE Data Types



Modified from PLoS Biol 9:e1001046, 2011

ENCODE Accomplishments

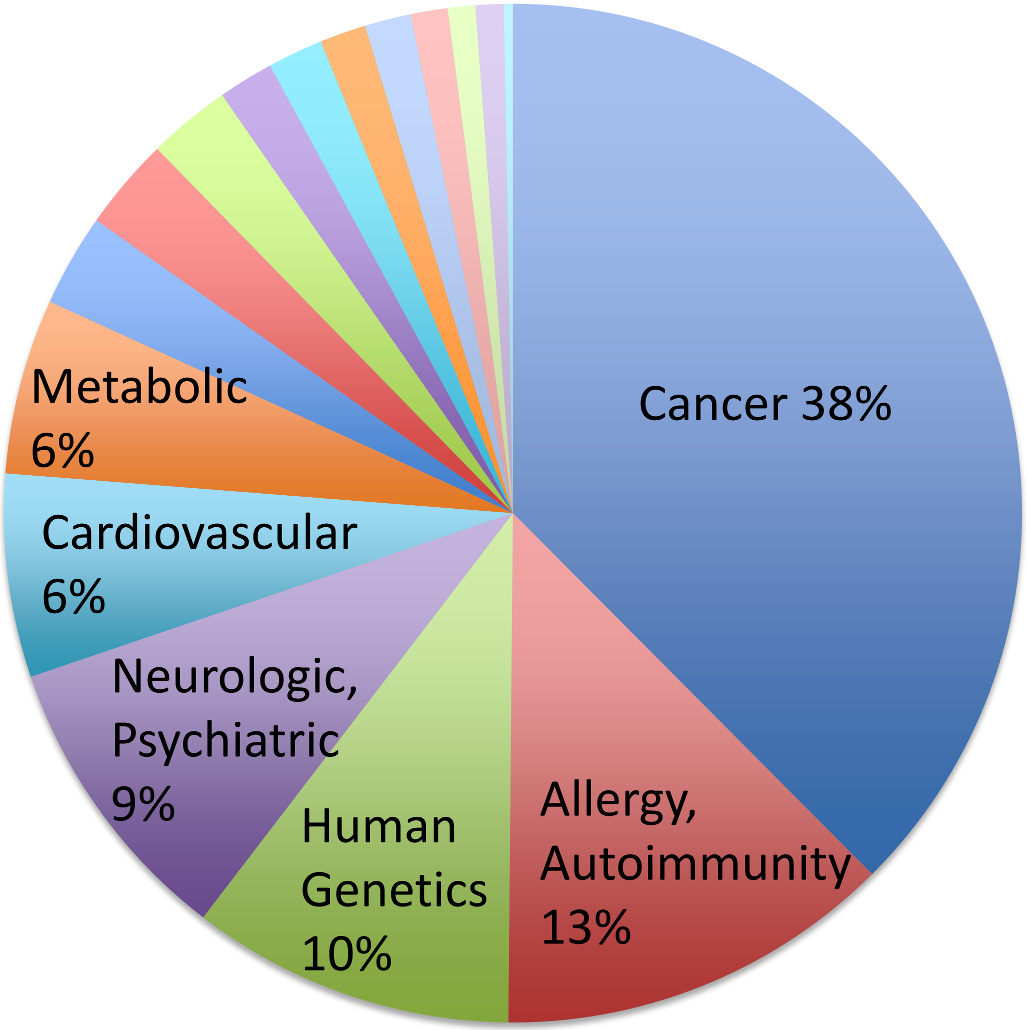
- Pre-publication release of data
  - High quality
  - Uniformly processed
- Sharing software
- Data interoperability
- Informed consent for unrestricted-access sharing of genomic data

Publications Using ENCODE Data

Hundreds of Consortium publications

~1000 community publications using ENCODE data:

- ~340 Human Disease
- ~500 Basic Biology
- ~170 Methods/Software Development



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Acknowledgments

- Workshop Organizing Committee:
  - Eric Boerwinkle, Carol Bult, John Lis, Aviv Regev
- NHGRI:
  - Eric Green, Jeff Schloss, Elise Feingold, Dan Gilchrist, Adam Felsenfeld, Carolyn Hutter, Rudy Pozzatti, Julie Coursen, Hannah Naughton, Alvaro Encinas, Kiara Palmer

Workshop Participants

- Technology, biological systems and diseases
- Independent investigators and consortia members
- NHGRI council and ENCODE External Consultants Panel
- ENCODE data users and ENCODE consortium members
- NHGRI, NIH, NIH intramural, and international funding

Workshop Objectives

1. (Scientific) Discuss the opportunities for understanding genome function through large-scale genomics studies.
2. (Implementation) Consider options for NHGRI projects that would address these opportunities.

Accessing Workshop Materials

- Workshop was video cast live
- Agenda, slides, and video are available at http://www.genome.gov/27560819
- Workshop report in a few weeks

Workshop Recommendations

- Continue genome-wide identification of functional elements
- Add functional characterization efforts
- Apply functional genomics assays directly to disease and biological studies
- Increase community participation
  - Community samples
  - Community data

Scientific Topics

- Background presentations and initial discussion
- Topic #1: Identifying and characterizing functional elements
- Topic #2: Using genomic assays of function to interpret disease-associated genetic variation
- Topic #3: Using genomic assays of function to study basic biological questions

Background Presentations And Initial Discussion

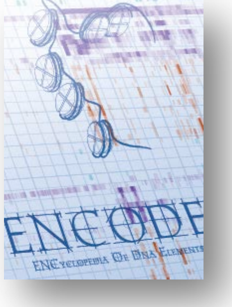
- ENCODE is very useful for studies of disease and biology (used in hundreds of publications)
- Systematic mapping in diverse cell types continues to be of high value
- Profiling cell types that are relevant to disease would be of high value
- Predictions of functional connections between regulatory elements and genes should be enhanced
- A systems biology approach is needed to advance the study of genome function

Topic #1: Identifying And Characterizing Functional Elements

- Unbiased mapping continues to have high value
- 3D interaction maps are needed to link regulatory elements to genes
- Single cell/low cell number assays are urgently needed
- Increased understanding of element functions is needed to determine causality
- Increased community participation
- Data standards, interoperability, and visualization tools are important

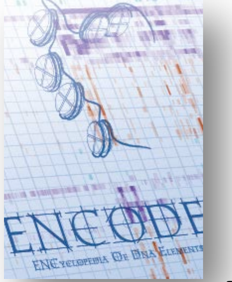
Topic #2: Functional Genomics And Disease

- Better understanding of the non-coding genome
- It is important to map and characterize genomic elements
- Some samples should be chosen in an unbiased manner, and others based on their importance in disease
- Better predictions of the effects of genetic variation on gene expression will aid disease studies
- Systems approaches are valuable for interpreting the function of genetic variants
- Increased sharing between the clinical and research enterprises is needed (this is inhibited by privacy rules)



Topic #3: Functional Genomics And Biology

- Systematic perturbations are needed to learn the connectivity of genes and regulatory elements
- Developing data standards and processing pipelines for new assays would have high value
- Functional characterization studies are needed to better understand the existing ENCODE data
- Incorporation of community samples and data is needed
- A gene-centric view could facilitate use of genomics by clinicians
- Some users require a set of standardized assays systematically applied across a wide range of cell types



Workshop Summary

- The highest priority is to expand beyond cataloging to understanding the function of genomic elements.
- This can be achieved by continued mapping efforts, a new functional characterization effort, increased community participation, and direct disease studies.
- This combination is expected to enhance genetic studies of human disease.

National Human Genome Research Institute